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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/733,485	12/08/2000	Erwin Ludo Roggen	6067.200-US	2466

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EXAMINER

WESSENDORF, TERESA D

ART UNIT	PAPER NUMBER
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1639

DATE MAILED: 05/19/2003

17

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/733,485

Applicant(s)

ROGGEN ET AL.

Examiner

T. D. Wessendorf

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE \_\_\_\_ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 10 March 2003.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 69 and 70 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 69-70 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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**DETAILED ACTION**

***Status of Claims***

Claims 1-20 have been cancelled in the present amendment (3/10/03). Claims 21-68 have been cancelled in the Preliminary Amendment of 12/8/00.

Newly added claims 69-70 are under examination.

***Claim Rejections - 35 USC § 112, first paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 69 and 70 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for DNA encoding a Savinase or Savinase library enzyme, does not reasonably provide enablement for the broadly claimed method using a gene encoding a diversified library of protein variants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for reasons advanced in the last Office action.

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Applicants state that the rejection under this statute has not been obviated by the newly added claims 69 and 70. However, these newly claims are also not commensurate in scope with the enabling disclosure provided in the specification. Therefore, the rejection of the last Office action is maintained, as applied to new claims 69 and 70, for essentially the same reasons set forth in the last action.

Claims 69-70 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification fails to provide an adequate written description of a method for selecting a variant protein with reduced immunogenecity by screening using competitive ELISA assay. In conjunction, there is no description in the specification as to a diverse DNA library of genes that encodes a variant protein. It does not describe how a diverse DNA library of genes is generated, the source of the diverse kinds of genes and/or identification of the genes for library formation. The description, particularly the EXAMPLES, which

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details the method used by applicants, describes a single, specifically known library, Savinase. Savinase is a trademark for a library. It is not readily apparent from the trademark or trade name as to the proper identity of the particular library material or product. The trademark does not identify the type of genes present in said trademark or the protein variants encoded by the genes or the means by which it is diversified. The EXAMPLES does not further describe screening by competitive ELISA assay. There are no steps for said competitive ELISA assay or the components present for a competitive assay. More importantly, there are no steps as to the selection or screening based on reduced immunogenecity rather, than the binding effect of the variants to an antibody.

***Claim Rejections - 35 USC § 112, second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

New claims 69-70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claim 69 is indefinite as to the screening step by which variants with reduced immunogenecity is determined by the antibody binding capacity by competitive ELISA assay, especially in the absence of positive teaching in the specification. The following terms: "reduced", "capacity" and "diversified" are relative terms which render the claim indefinite. These terms are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. "The samples" lack antecedent support from the preceding statement. This is a different concept from the preceding step of "sampling each cell culture".

The use of variants and diversity of the protein library, within the claimed context, provides for confusion and ambiguity as to whether these are different or the same.

#### ***Double Patenting***

Claims 69 and 70 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 55-73 of copending Application No. 09/417,608 ('608 application) or over claims 1-7, 11-14, 20-21 and 40 of copending Application No. 09/695,173 ('173 application). Although the conflicting claims are not

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identical, they are not patentably distinct from each other because of the reasons set forth in the last Office action.

***Response to Arguments***

Applicants submit that this rejection is premature since both the copending applications have not yet been allowed. As stated in the last Office action, the rejection is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented. In the absence of terminal disclaimer, the rejection is maintained.

[It is noted that applicants have filed several applications having one or more common inventors that appears to claim the same invention except worded differently. Applicants are required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822].

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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Claims 69-70 are are rejected under 35 U.S.C. 102(b) as being anticipated by Jespers et al (J. Mol. Biol.) or Collen et al (WO 96/21016) for reasons stated in the last Office action.

***Response to Arguments***

Applicants admit that Jespers discloses a method of epitope mapping, comprising preparing a randomized library of staphylokinase mutants by error-prone PCR, phage display and negative selection on binding to antibodies. But argue that Jespers does not disclose a method comprising the use of competitive ELISA to identify variants with reduced immunogenicity. As best as the claims can be interpreted i.e., reduced immunogenicity is determined by antibody (ab) binding capacity by competitive ELISA assay, Jespers discloses the same ELISA method at page 708 where the mutants compete with each other for binding to antibody as measured by ELISA. See further the paragraph bridging pages 713-714 as to the mutated Sak-phages selected with reduced antibody recognition with retention of plasminogen binding activity. See the detailed steps disclosed at page 714, col. 1 up to page 716, col.2.

The arguments under Jespers apply to the Collen et al reference. Applicants used the same arguments as in Jespers for the Collen reference.



Claim 69 is rejected under 35 U.S.C. 102(b) as being anticipated by Williams et al (Jrnl. of Immunological Methods) for reasons advanced in the last Office action.

Applicants recognize that the method of Williams raises an antibody against BLG and subjects a library of randomized short peptides to the antibody. But argue that Williams does not disclose a method comprising the use of competitive ELISA to identify variants with reduced immunogenecity. As best as the claims can be interpreted i.e., reduced immnogenecity is determined by antibody (ab) binding capacity by competitive ELISA assay. Williams discloses the ELISA assay method at e.g., page 1, the abstract.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 69-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Jespers et al (J. Mol. Biol.) or

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Williams et al (Jrnl. of Immunological Methods) or Collen et al (WO 96/21016) for reasons of record.

Because the claims are subject to several interpretations, it is considered that each of the references above renders the claimed competitive ELISA assay obvious. It would have been obvious to one having ordinary skill in the art at the time the invention was made to use competitive ELISA for the different mutants present in the library. The different mutants or variants (as claimed) can compete with one another for binding to the antibody. The binding effect can result in reduce antigenecity for some of the mutants, as disclosed by e.g., Jespers. The reduction in the antigenecity effect is obviously the claimed reduction in immunogenecity.

No claim is allowed.

#### **Conclusion**

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS

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of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action.. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

**REASSIGNMENT OF LOCATION**


The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit **1639**.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (703) 308-3967. The examiner is normally on Flexitime.

The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-7924 for regular communications and (703) 308-7924 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

  
T. D. Wessendorf  
Primary Examiner  
Art Unit 1627

tdw

May 15, 2003